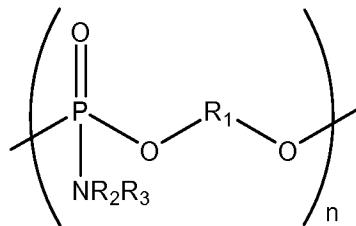


CLAIM LISTING

Claim 1 (currently amended): A water soluble and positively charged biodegradable polyphosphoramidate that is capable of forming a complex with negatively charged bioactive macromolecules in aqueous solutions and comprises the recurring monomeric unit shown in Formula I:

**FORMULA I**

wherein

R_1 is a divalent aliphatic organic moiety;

R_2 and R_3 are each independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, or heteroalicyclic, cycloalkyl, aralkyl, or cycloalkylalkyl groups;

each non-hydrogen occurrence of R_2 and R_3 is substituted with one or more positively charged groups; and

n is from 20 to 2,000;

wherein when if R_1 is $-(CH_2)_a-$ and one of R_2 and R_3 is hydrogen, the other of R_3 and R_2 is not an alkyl group selected from the group consisting of hydrogen, aryl, heteroaryl, heteroalicyclic, cycloalkyl, aralkyl, cycloalkylalkyl,

wherein a ranges from 2 to 6.

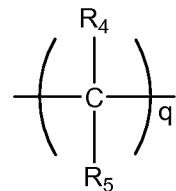
Claim 2 (original): A positively charged biodegradable polyphosphoramidate of claim 1, wherein the biodegradable polyphosphoramidate has between about 20 and about 2,000 phosphoramidate groups.

Claim 3 (cancelled)

Claim 4 (original): A positively charged biodegradable polyphosphoramidate of claim 2, wherein one or more of R_1 , R_2 , or R_3 is substituted with one or more groups capable of facilitating intracellular delivery of a negatively charged bioactive macromolecules, selected from the group consisting of lysosomalytic agent, an amphiphilic peptide, or a steroid derivative.

Claim 5 (previously presented): A positively charged biodegradable polyphosphoramidate of claim 4, wherein the group capable of facilitating intracellular delivery of negatively charged bioactive macromolecules is a cholesterol group.

Claim 6 (previously presented): A positively charged biodegradable polyphosphoramidate of claim 1, wherein R_1 is defined in Formula II:



FORMULA II

wherein each occurrence of R_4 and R_5 are independently selected from the group consisting of hydrogen or alkyl group; and

q is 2 to 4.

Claim 7 (withdrawn): A positively charged biodegradable polyphosphoramidate composition formed by complexation in aqueous solutions comprising:

- (a) at least one negatively charged bioactive macromolecule; and
- (b) a water soluble and positively charged biodegradable polyphosphoramidate of

claim 1.

Claim 8 (withdrawn): A method of preparing complexes or nanoparticles comprising of water soluble, positively charged biodegradable polymer of Formula I and at least one negatively charged macromolecules comprising the steps of:

mixing an aqueous solution of the positively charged biodegradable polymer of Formula I with concentrations ranging from 1 $\mu\text{g}/\text{ml}$ to 500 $\mu\text{g}/\text{ml}$,

with an aqueous solution of one or more bioactive macromolecule, one of which is negatively charged macromolecule and is able to complex with polymer of Formula I.

Claim 9 (withdrawn): A method of preparing complexes or nanoparticles of claim 8, comprising of water soluble, positively chargeable biodegradeable polymer of Formula I and at least one negatively charged bioactive macromolecule, wherein the negatively charged or neutral bioactive macromolecules are selected from the group consisting of DNA, RNA, proteins, and polysaccarides.

Claim 10 (withdrawn): A method of preparing complexes or nanoparticles of claim 8 and 9, wherein the biodegradeable polymer is capable of complexing 20-60% by weight of the negatively charged bioactive macromolecules.

Claim 11 (withdrawn): A method of preparing a positively charged biodegradable polyphosphoramidate of claim 10, wherein the biodegradable polyphosphoramidate has between about 20 and about 200 phosphoramidate groups.

Claim 12 (withdrawn): A method of preparing a positively charged biodegradable polyphosphoramidate composition of claim 7, comprising the steps of:

mixing an aqueous solution of the positively charged biodegradable polymer of Formula I with concentrations ranging from 1 $\mu\text{g}/\text{ml}$ to 500 $\mu\text{g}/\text{ml}$,

with an aqueous solution of one or more biological active macromolecules, which is able to complex with polymer of Formula I.

Claim 13 (withdrawn): A method of preparing a positively charged biodegradable polyphosphoramidate composition of claim 12, wherein the negatively charged or bioactive macromolecules are selected from the group consisting of DNA, RNA, proteins, and polysaccharides.

Claim 14 (withdrawn): A method of preparing a positively charged biodegradable polyphosphoramidate composition of claim 12 or 13, wherein the biodegradable polyphosphoramidate is capable of complexing 20-60% by weight of the negatively charged bioactive macromolecules.

Claim 15 (withdrawn): A method of preparing a positively charged biodegradable polyphosphoramidate composition of claim 12 or 13, wherein the biodegradable polyphosphoramidate has between about 20 and about 200 phosphoramidate groups.

Claim 16 (withdrawn): A method for the controlled release of a bioactive macromolecule comprising the steps of:

providing a positively charged biodegradable polyphosphoramidate composition of claim 7, and

contacting the composition in vivo or in vitro with a biological fluid, cell or tissue under conditions conducive to the delivery of at least a portion of the biologically active substance to the biological fluid, cell or tissue so that the biologically active substance is released in a controlled manner.

Claim 17 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is released in-vivo.

Claim 18 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is released in-vitro.

Claim 19 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is released extracellularly.

Claim 20 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is released intracellularly.

Claim 21 (withdrawn): A method of claim 16, wherein the bioactive macromolecule(s) are selected from the group consisting of DNA, RNA, proteins, and polysaccharides.

Claim 22 (withdrawn): A method of claim 16, wherein the biodegradable polymer is capable of complexing 20-60% by weight of the negatively charged bioactive macromolecule.

Claim 23 (withdrawn): A method of claim 16, wherein the biodegradable polymer has between about 20 and about 200 phosphate groups.

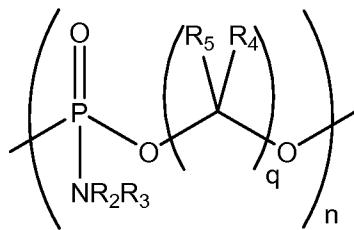
Claim 24 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is a growth factor.

Claim 25 (withdrawn): A method of claim 16, wherein the bioactive macromolecule is selected from the group consisting of DNA sequences, genes, gene fragments, DNA encoding vaccines, therapeutic agents, cytokines, immunoadjuvants, cancer therapeutic agents, proteins, and combinations thereof.

Claim 26 (withdrawn): A method of claim 25, wherein DNA sequence, gene or gene fragment is administered in connection with gene therapy.

Claim 27 (withdrawn): A method of any one of claims 17 through 26 wherein the positively charged biodegradable polyphosphoramidate composition, including complexes or nanoparticles is delivered *in vivo*.

Claim 28 (withdrawn—currently amended): A composition comprising a water soluble and positively charged biodegradable polyphosphoramidate that is capable of forming a complex with negatively charged bioactive macromolecules in aqueous solutions having a recurring monomeric unit shown in Formula III:

**FORMULA III**

wherein

R_1 is a divalent aliphatic organic moiety;

R_2 and R_3 are each independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, or heteroalicyclic, cycloalkyl, aralkyl, or cycloalkylalkyl groups;

each non-hydrogen occurrence of R_2 and R_3 is substituted with one or more positively charged groups;

R_4 and R_5 are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxy, aryl, heteroaryl, heteroalicyclic, aralkyl, and a steroid derivative;

q is from about 1 to about 5; and

n is from about 20 to about 2,000.

Claim 29 (withdrawn): The composition of claim 1, wherein the biodegradable polyphosphoramidate has between about 20 and about 2,000 phosphoramidate groups.

Claim 30 (withdrawn): The composition of claim 1, wherein non-hydrogen occurrences R_2 and R_3 are substituted with one or more charged groups selected from the group consisting of primary amine, secondary amine, tertiary amine, quaternary amine, or imidazoyl.

Claim 31 (withdrawn): The composition of claim 2, wherein one or more of R_1 , R_2 , or R_3 is substituted with one or more groups capable of facilitating intracellular delivery of a negatively charged bioactive macromolecules, selected from the group consisting of lysosomalolytic agent, an amphiphilic peptide, or a steroid derivative.

Claim 32 (withdrawn): The composition of claim 4, wherein the group capable of facilitating intracellular delivery of negatively charged bioactive macromolecules is a cholesterol group.

Claim 33 (new): The positively charged biodegradable polyphosphoramidate of claim 1, wherein non-hydrogen occurrences R₂ and R₃ are substituted with one or more charged groups selected from the group consisting of primary amine, secondary amine, tertiary amine, quaternary amine or imidazoyl.